B. Resp nse to Office Action

Responsive to the Office Action mailed August 28, 2001 in the above matter, restriction was required to the following allegedly distinct inventions:

I. Claims 1-16, 43, and 44-47 drawn to microparticles and compositions comprising microparticles.

II. Claim 17-37, drawn to a methods of making microparticles and microparticle compositions.

III. Claims 38, 40 and 49 drawn to methods of treatment of disease.

IV. Claims 39 and 48, drawn to use of a microparticle for diagnosis of disease.

V. Claims 41, 42, 50 and 51, drawn to use of a microparticle as a vaccine or for raising an immune response.

Applicants elect the Group I claims, with traverse, for initial prosecution on the merits. (In view of the above claim amendments, this group corresponds to presently pending claims 1-7, 9-16, 43-47, 52-59.)

This election is made with traverse. Examination of earlier filed International application No. PCT/US99/17308 indicated unity of invention among claims 1-51. The as-filed claims in this national stage application correspond to those claims. Hence, it is respectfully submitted that restriction is improper.

Pursuant to 35 U.S.C. 121, election of a single disclosed species for prosecution on the merits is also required, even though the restriction requirement is traversed. Applicants hereby elect a polynucleotide as species for the first biologically active macromolecule. Applicants further elect an adjuvant as species for the second biologically active macromolecule.

CONCLUSION

Applicants submit that claims 1-7, 9-19 and 21-68 are in condition for allowance, early notification of which is earnestly solicited. The Examiner is encouraged to

telephone the Applicant's attorney at (703) 433-0510 in order that any outstanding issues be resolved.

FEES

The Office is authorized to charge the $920.00 three-month extension fee, as well as any other fees required to deposit account number 50-1047.

Respectfully submitted,

David B. Bonham
Registration No. 34,297

Attorney for Applicant
Mayer Fortkort & Williams, PC
251 North Avenue West, 2nd Floor
Westfield, NJ 07090
Tel.: 703-433-0510
Fax: 703-433-2362

I certify that this document is being deposited on December 27, 2001 with the U.S. Postal Service with sufficient postage as first class mail under 37 C.F.R. 1.8 in an envelope addressed to: Assistant Commissioner for Patents, Box FEE, Washington, D.C. 20231.

Marjorie Scariati
(Printed Name of Person Mailing Correspondence)

(Signature)

Version With Markings To Show Changes Made

IN THE CLAIMS:

1. A microparticle having an adsorbent surface, said microparticle comprising:

a polymer selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate; and

a cationic or anionic detergent.

2. The microparticle of claim 1, further comprising a first biologically active macromolecule adsorbed on the surface thereof, wherein the first biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, ~~a pharmaceutical~~ a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

3. The microparticle of claim 2, further comprising a second biologically active macromolecule encapsulated within said microparticle, wherein the second biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, ~~a pharmaceutical~~ a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

~~8. The microparticle of any of claims 1-5, wherein the detergent is an nonionic detergent.~~

9. The microparticle of any of claims ~~2-8~~ 2-7, wherein the first biologically active macromolecule is an antigen selected from the group consisting of gp120, gp160, p24gag, p55gag, and Influenza A hemagglutinin antigen.

10. The microparticle of any of claims ~~2-9~~ 2-7, wherein the first biologically active macromolecule is a polynucleotide which encodes gp120.

11. The microparticle of any of claims ~~3-10~~ 3-7, 9 and 10, wherein the second biologically active macromolecule is an adjuvant.

12. The microparticle of claim 11, ~~any of claims 1-11,~~ wherein the adjuvant is an aluminum salt.

13. A microparticle composition comprising a microparticle of any of claims ~~1-12~~ 1-7 and 9-12 and a pharmaceutically acceptable excipient.

14. A microparticle composition comprising a microparticle according to any of claims ~~1-13~~ 1-7, 9, 10 and 13, further comprising an adjuvant.

17. A method of producing a microparticle having an adsorbent surface, said method comprising the steps of:
(a) dispersing a mixture of a polymer solution and a cationic or anionic detergent, wherein the polymer solution comprises a polymer selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present in the mixture at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1; and

(b) removing the organic solvent from the emulsion.

~~20. The method of claim 17 wherein the detergent is a nonionic detergent.~~

21. The method of any of claims ~~17-20~~ 17-19 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.0001:1 to about 0.01:1.

22. The method of any of claims ~~17-20~~ 17-19 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.001:1 to about 0.01:1.

23. The method of any of claims ~~17-20~~ 17-19 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.005:1 to about 0.01:1.

24. The method of any of claims ~~17-23~~ 17-19 and 21-23, wherein the microparticle comprises a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

27. A method of producing a microparticle having an adsorbent surface to which a biologically active macromolecule has been adsorbed, said method comprising the steps of:

(a) emulsifying a mixture of a polymer solution and a cationic or anionic detergent to form an emulsion, wherein the polymer solution comprises a polymer selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present in the mixture at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1;

(b) removing the organic solvent from the emulsion, to form said microparticle having the adsorbent surface; and

(c) adsorbing the macromolecule to the surface of the microparticle.

29. The method of any of claims 27-28, wherein the macromolecule is an antigen selected from the group consisting of gp120, gp160, p24gag, p55gag and Influenza A hemagglutinin antigen.

34. A microparticle made according to the method of any of claims ~~17-33~~ 17-19 and 21-33.

36. A method of producing a microparticle composition comprising a microparticle having an adsorbent surface to which a biologically active macromolecule has been adsorbed, said method comprising the steps of:

(a) emulsifying a mixture of a polymer solution and a cationic or anionic detergent to form an emulsion, wherein the polymer solution comprises a polymer selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1;

(b) removing the organic solvent from the emulsion, to form said microparticle having the adsorbent surface;

(c) adsorbing the macromolecule to the surface of the microparticle; and

(d) combining the microparticle having the adsorbed macromolecule from step (c) with a pharmaceutically acceptable excipient to form said microparticle composition.

43. A microparticle having an adsorbent surface, said microparticle comprising:

a biodegradable polymer; and

a cationic or anionic detergent.

44. The microparticle of claim 43, further comprising a first biologically active macromolecule adsorbed on the surface thereof, wherein the first biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, ~~a pharmaceutical~~ a

pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

52. The microparticle of claim 7, wherein the first biologically active macromolecule is a polypeptide.

53. The microparticle of claim 52, wherein the first biologically active macromolecule is a polypeptide antigen selected from the group consisting of HIV antigens, hepatitis C virus antigens, and influenza A virus antigens.

54. The microparticle of claim 6, wherein the first biologically active macromolecule is a polynucleotide.

55. The microparticle of claim 54, wherein the polynucleotide encodes an antigen.

56. The microparticle of claim 55, wherein the polynucleotide encoding the antigen is a plasmid DNA molecule.

57. The microparticle of claim 55, wherein the antigen is selected from the group consisting of HIV antigens, hepatitis C virus antigens, and influenza A virus antigens.

58. The microparticle of claim 6, wherein the cationic detergent is hexadecyltrimethylammonium bromide.

59. The microparticle of claim 7, wherein the anionic detergent is sodium dodecyl sulfate.

60. The method of claim 27, wherein the detergent is an anionic detergent.

61. The method of claim 60, wherein the macromolecule is a polypeptide.

62. The method of claim 61, wherein the polypeptide is a polypeptide antigen selected from the group consisting of HIV antigens, hepatitis C virus antigens, and influenza A virus antigens.

63. The method of claim 27, wherein the detergent is a cationic detergent.

64. The method of claim 63, wherein the macromolecule is a polynucleotide.

65. The method of claim 64, wherein the polynucleotide encodes an antigen.

66. The method of claim 65, wherein the polynucleotide encoding the antigen is plasmid DNA.

67. The method of claim 65, wherein the antigen is selected from the group consisting of HIV antigens, hepatitis C virus antigens, and influenza A virus antigens.

68. Use of a microparticle composition of claim 51, wherein said immune response comprises a CTL immune response.